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| APPLICATION NUMBER | FILING DATE | FIRST NAMED APPLICANT | ATTY. DOCKET NO. |
|---|---|---|---|
| 08/700737 | | | |
| 08/700,737 | 08/15/96 | PONATH | P LKS95-10 |

EXAMINER

HM11/0313

| ART UNIT | PAPER NUMBER |
|---|---|
| BAEIN, E | 12 |
| 1644 | |

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DATE MAILED: 03/13/98

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

## OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 12/12/97

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire —3— month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

**Disposition of Claims**

☒ Claim(s) 1-9 and 11-45 is/are pending in the application.
Of the above, claim(s) 16, 17, 21, 22, 25, 26, and 29-45 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 1-9, 11-15, 18-20, 23, 24, 27, and 28 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

**Application Papers**

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

☒ Notice of Reference Cited, PTO-892
☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

★ U.S. GPO: 1998-404-496/40051

## DETAILED ACTION

1. The examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1644.

2. The request filed 3/15/99 (Paper No. 15) for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/700,737 is acceptable and a CPA has been established An Action on the CPA follows.

Applicant's amendment, filed 3/15/99 (Paper No. 16), is acknowledged.
Claims 1, 8, 13 and 18 have been amended.

Applicant's amendment, filed 5/10/99 (Paper No. 19), is acknowledged.
Claims 1, 8, 13 and 18 have been amended.

A restriction was required under 35 USC § 121 in the parent application, Paper No. 7 between one of the following Groups:

I. Claims 1-15, 18-20, 23-24 and 27-28, drawn to a humanized α4β7-specific antibodies.
II. Claims 16-17, 21-22, 25-26 and 29-40, drawn to nucleic acids, vector and host cells.
III. Claims 41-45, drawn to a method of treatment with α4β7-specific antibodies.

Applicant elected Group I, claims 1-3 with traverse. This restriction requirement is hereby reiterated. Accordingly, claims 16-17, 21-22, 25-26 and 29-45 stand withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a nonelected inventions.

Claim 10 has been canceled previously.

Claims 1-9, 11-15, 18-20, 23-24 and 27-28 are being acted upon presently.

3. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action. This Office Action will be in response to applicant's arguments, filed 3/15/99 (Paper No. 16). The rejections of record can be found in previous Office Actions (Paper Nos. 7/12).

Applicant's request for an Interview is acknowledged. The examiner phoned applicant's representative Helen Wendler on 7/13/99 to indicate that an Office Action was forthcoming and that an Interview would be granted upon request.

4. Formal drawings and photographs have been submitted which fail to comply with 37 CFR 1.84. Please see the form PTO-948 previously sent in Paper No. 7.

5. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Applicant is required to identify the nucleotide and amino acid sequences in the specification with SEQ. ID NOS.

Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate corrections are required

6. Claims 1-9, 18-20, 23-24 and 27-28 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-9, 18-20, 23-24 and 27-28 are indefinite in the recitation of "substantially the same" because the metes and bounds of this phrase is not clear. This "limitation" is a relative phrase renders the claim indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear as to which structural or functional properties are being relied upon and to what extent.

B) Claims 8,9,11,12 and 28 are indefinite in the recitation of "has the sequence" or "having the sequence" because it is unclear whether the transitional phrases "has" and "having" are meant to be open (i.e. comprising) or closed (i.e. consisting of). Applicant is required to amend the claims to recite standard transitional phrases for clarity.

C) The applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

8. Claims 1-4, 6, 8-9, 13 and 18 are rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over Bendig et al. (U.S. Patent No. 5,840,299; 1449) (see entire document). Bendig et al. teaches humanized α4-specific antibodies. Although the references does not teach the αβ7 specificity per se, it appears that the referenced antibodies have binding specificities encompassed by the claimed invention. Given the broadest reasonable interpretation of "substantially the same" and "compete"; again the referenced antibodies appears to have binding specificities encompassed by the claimed invention. The burden is on the applicant to establish a patentable distinction between the claimed and referenced antibodies/methods. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980) and Ex parte Phillips, 28 USPQ2d 1302 (BPAI 1993).

9. Claims 1-9, 18-20, 23-24 and 27-28 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Queen et al. (U.S. Patent No. 5,530,101) in view of Lazarovits et al. (J. Immunol. 151: 6482-6489, 1993) and in further evidence by the Information for Contributors for this Volume of the Journal of Immunology essentially for the reasons of record set forth in Paper Nos. 7/12

Applicant's arguments, filed 3/15/99 (Paper No. 16), have been fully considered and are not found convincing essentially for the reasons of record.

Applicant argues that absent a teaching of the variable region of the Act-1 antibody, applicant's invention is not obvious. Applicant argues that Lazarovits et al. Do not suggest the use of Act-1 for immunotherapy, however acknowledge this reference teaching the possible benefit of interfering with $\alpha 4\beta 7$ for immunotherapy of arthritis (page 6487, column 1). Applicant argues that Queen et al. Describe general humanization procedures but do not direct the ordinary artisan to Act-1.

Applicant further agues in conjunction with Bell and Deuel that the instant invention is not obvious based upon the general teachings of humanizing antibodies and no art teaching of the sequence of the variable regions of the Act-1 antibody. Also, applicant argues that the prior art neither teaches nor suggests the sequences of the light/heavy/CDR sequences of the Act-1 antibody nor the particular structure claimed.

This proposition that the references failed to teach the structure of the claimed antibody precludes the teachings thereof from serving as evidence to establish a prima facie case of obviousness is contrary to a body of law which holds that a product may be described by the process of making it. As pointed in Ex parte Goldgaber, 41 USPQ2d 1173, 1176 (BPAI 1996), there is nothing intrinsically wrong in the application of methodology in the rejection product claims under 35 USC 103 depending on the particular facts of the case, the manner and context in which methodology applies and the overall logic of the rejection. Nor does Bell or Deuel issue a blanket prohibition against the application of methodology in rejecting product claimed defining DNA of cDNA. It is perfectly acceptable to consider the method by which a compound is made in evaluating the obviousness of the compound. In determining obviousness, it is appropriate to consider such matters as the manner of preparation of the composition vis-a-vis the prior art, the structural similarities as well as differences between the claimed composition and that of the prior art and the presence or absence of properties which would unobvious in view of the prior art. As noted in In re Cofer, 354, F.2d 664, 148 USPQ 268 (CCPA 1966), the particular structure or form of a chemical compound is an important consideration in determining obviousness under 35 USC 103; but it is not the only consideration.. A compound may well be defined or described by characteristics other than its chemical structure.

As set forth in the prior art rejections; the selection process for desired properties is critical in the isolation of an antibody of interest. Though those skilled in the art may be unaware of the exact chemical structure of an antibody (e.g. amino acid or nucleic acid sequence), they are aware that it is composed of established relatively unchanging array of nucleotides and amino acids which code for the particular immunoglobulin. Importantly, they are also aware that the art known immunoglobulin probes would have been able to isolate the targeted antibody or immunoglobulin of interest. For example, one does not need to determine the amino acid sequence of a rearranged V (variable) region before cloning, as evidenced by Queen et al.. Similarly, the instant application has relied upon heavy and light chain probes to identify and isolate the claimed antibody species. In fact, it appears that applicant has relied upon a commercial kit to

clone Act-1 (for example, see Example 1 of the instant specification). No specific probes were required to isolate Act-1 at the time the invention was made, provided that one screened for the desired biological properties, which relied upon the isolation of desired antibodies having high affinity and complementarity with the α4β7 specificity and therefore structure. Immunoglobulin gene structure and organization were well understood in the art at the time the claimed invention was made and that strategies for cloning the DNAs encoding immunoglobulin variable regions genes were well established in the art at the time the claimed invention was made, as were methods for the production of DNA constructs comprising expression vectors containing DNAs encoding immunoglobulin variable regions. The determination and manipulation of the amino acid and nucleic acid sequence is an outcome and mechanism of such engineering. The art known procedures of making humanized antibodies enable the ability of the ordinary artisan at the time the invention was made to derive a humanized antibody that binds to α4β7 and encompasses the claimed limitations including "substantially the same", "competes with murine Act-1" or "derived from Act-1" including the specific structures claimed.

The rejections of record clearly set forth motivation and a reasonable expectation of success in deriving humanized α4β7-specific antibodies, including those that are substantially the same as or compete with Act-1. In addition, it was known in the prior art that humanized antibodies to antigens of interest could be useful in a variety of modalities, including therapy as well as diagnostics and assays (see Queen et al., particularly columns 18-20). Also, antigen-binding fragments were known and used at the time the invention was made for the same or similar modalities encompassing therapeutics, diagnostics and assays.

With respect to humanizing Act-1 itself; applicant has not provided any objective evidence that the Act-1 antibody/hybridoma was not available to others at the time the invention was made. It is noted the inventive entity of the instant application does not recite the authors/investigators who made and used the Act-1 antibody as relied upon in the prior art of record (Lazarovits et al., J. Immunol. 151: 6482, 1993) nor the first reference citing the construction of the Act-1 antibody (Lazarovits et al. J. Immunol. 133: 857, 1984; cited as reference 32 of the prior art reference and on page 2 of the instant specification as well as reference #AS on the 1449). Also, it is noted that Information for Contributors to the Journal of Immunology are expected to provide unique materials to qualified investigators. Therefore, it appears that the Act-1 antibody/hybridoma was available to others at the time the invention was made.

Therefore, applicant's reliance upon claiming discrete sequences for the α4β7 /Act-1-specific humanized antibodies are also met by the prior art teachings.

Therefore, the combined references provide motivation with an expectation of success in deriving humanized α4β7 /Act-1-specific antibodies. Therefore, from the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention was a whole is prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not persuasive and the rejection is maintained

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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Group 1640
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July 13, 1999

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